Case Lessons 40-2025

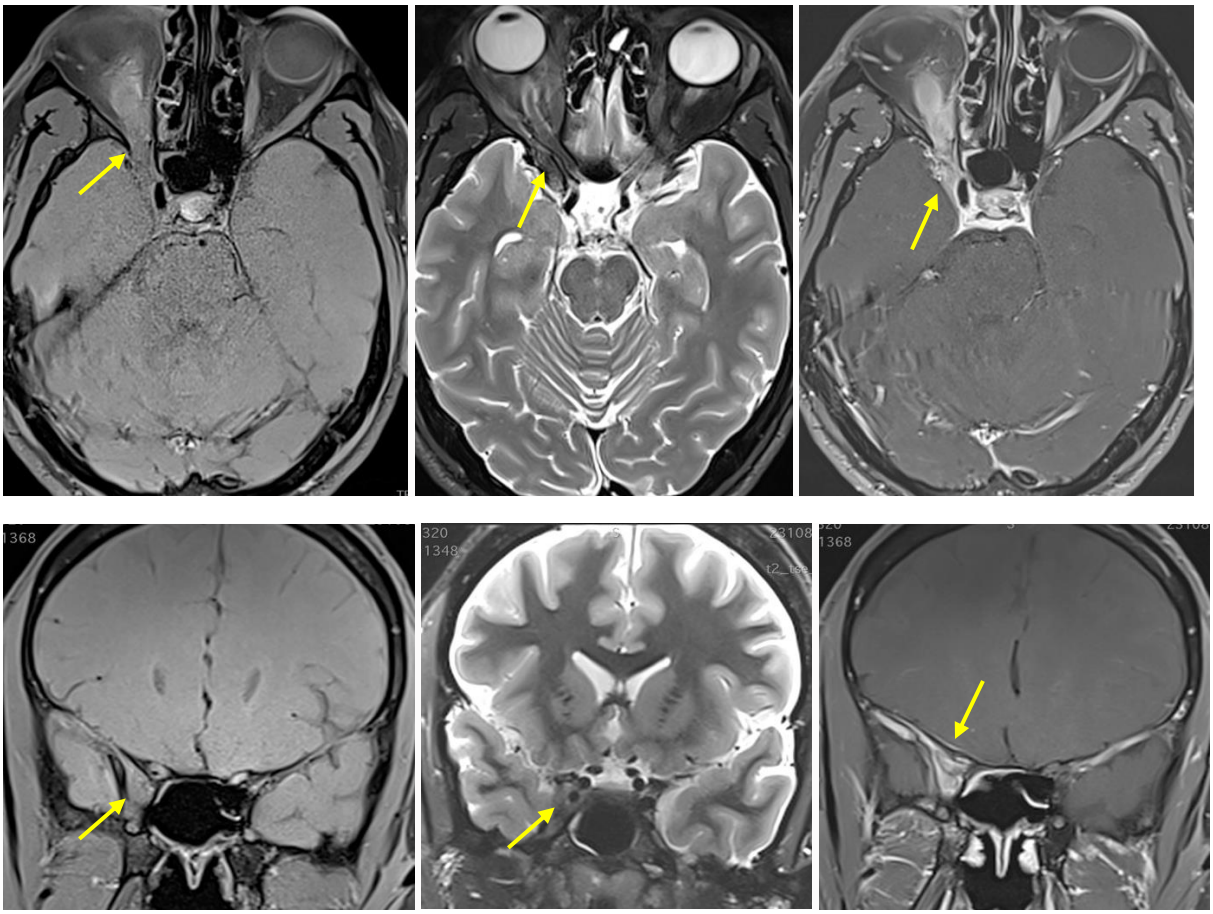
Tolosa Hunt Syndrome: A Case Series

Stela Dodaj, Mirel Grada, Vojsava Leka, Aida Agastra, Eugen Enesi, Arben Rroji, Mentor Petrela

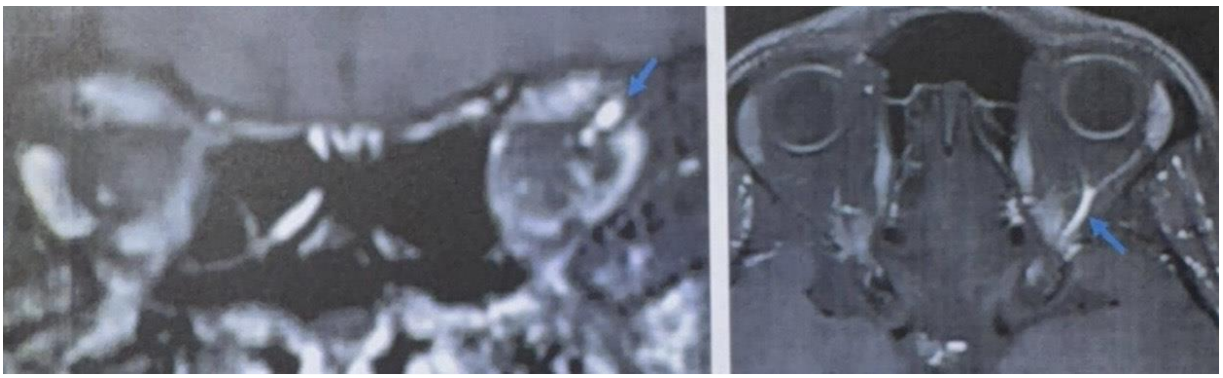
Introduction: Tolosa Hunt Syndrome (THS) is a rare medical condition with an incidence of 1 case per million, characterized by idiopathic granulomatous inflammation of the cavernous sinus and/or the superior orbital fissure, potentially extending to the orbital apex. It typically manifests as painful ophthalmoplegia, and about half of the patients experience recurrent episodes at intervals of months or years [1, 2]. Diagnosis relies on specific criteria, which include the presence of consistent, dull, retro-orbital pain, paresis of the third, fourth or sixth cranial nerves, as well as the first branch of the trigeminal nerve, symptoms that can last from several days to weeks, and the absence of structures involvement outside the cavernous sinus. THS is primarily a diagnosis of exclusion, determined through clinical presentation and the patient`s response to steroid treatment. [3].

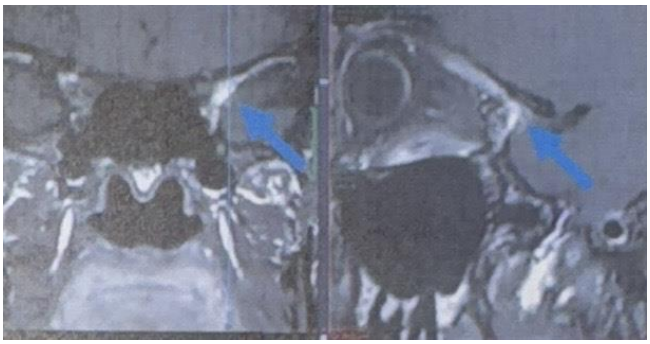
We present three Albanian patients of confirmed Tolosa Hunt syndrome.

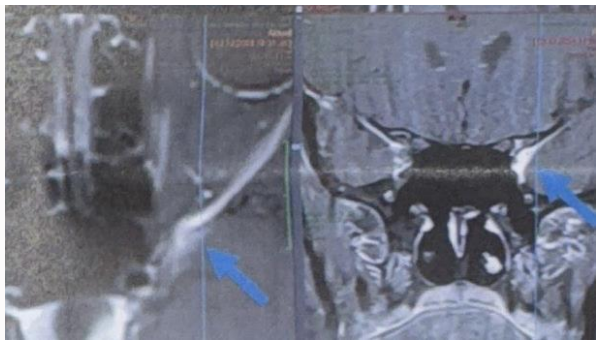
Case 1: 36-year-old male with continuous right hemicrania, partial ophthalmoplegia with horizontal diplopia. All laboratory tests showed no abnormality. MRI showed dural thickness and contrast enhancement of right cavernous sinus. Medication with corticosteroids was started and good clinical outcome was evident during the treatment. But, once the medication was stopped, relapse of the symptoms happened. Therefore, being corticosteroid dependent, long term low dose prednisone was decided.



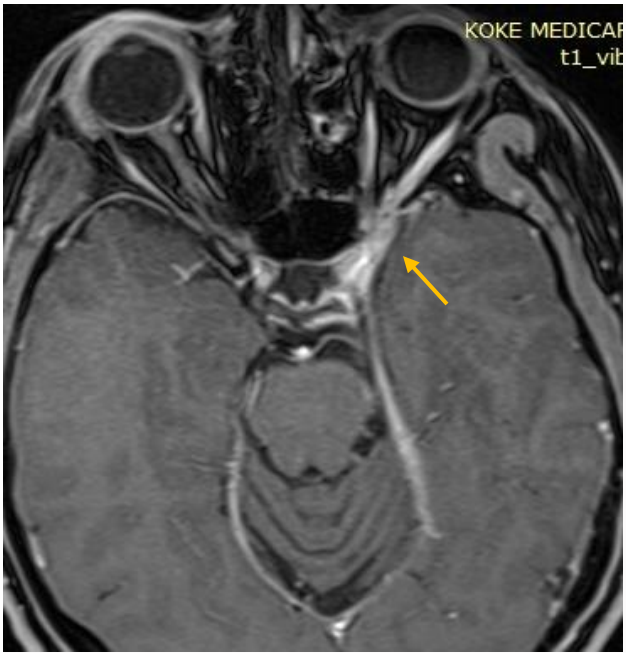
Case 2: 48-year-old female with one-week history of high intensity shooting precisely localized, left supraorbital-temporal headache lasting for seconds, left ophthalmoplegia and diplopia. She reported that double vision was a progressing concern that had started two months ago. Her past medical history revealed hypothyroidism and migraine. This type of headache of the last week was different in characteristics from migraine attacks. Other laboratory tests were normal. Treatment with corticosteroids and anticoagulant was started with tapering for one month and clinical improvement was noted. No other relapses were reported.







Case 3: 26-year-old female with three weeks history of progressive left periorbital headache and third nerve palsy. She reported that she had the same symptoms but milder ten months ago, but didn`t consult any clinician. MRI revealed dural thickness and contrast enhancement of cavernous sinus walls. Infectious, autoimmune and other laboratory tests were normal. Treatment with oral corticosteroids was started and tapered for three months and clinical improvement was seen



Discussion: According to the third edition of the International Classification of Headache Disorders (ICHD-3), the diagnosis of THS requires unilateral headache associated with one or more ipsilateral oculomotor nerve palsies (cranial nerves III, IV, and/or VI), supported by MRI or biopsy evidence of granulomatous inflammation and the exclusion of other causes of painful ophthalmoplegia [4]. Clinically, THS presents with orbital or periorbital headache that precedes or accompanies ophthalmoplegia, and its manifestations may resemble those of recurrent

painful ophthalmoplegic neuropathy, particularly a condition that typically begins in childhood and involves ocular motor nerves [5]. As a diagnosis of exclusion, THS requires careful assessment to rule out brainstem and peripheral nerve lesions, as well as vascular, neoplastic, and infectious etiologies. Additional involvement of the ophthalmic and maxillary branches of the trigeminal nerve supports localization to the cavernous sinus, whereas visual impairment suggests optic nerve involvement [6]. Histopathologically, THS is associated with lymphocytic and plasma cell infiltration and thickening of the cavernous sinus dura mater.

MRI has been found to be the most valuable imaging technique to distinguish THS from other THS-like entities and offers a precise assessment, management, and therapeutic planning of the underlying pathological conditions. MRI features suggestive of CS involvement in THS include enlargement and dural margin convexity, with or without abnormal tissue, which is isointense with gray matter on T1-weighted images and isointense to slightly hypointense on T2-weighted sequences. The abnormal tissue enhances markedly with contrast. There may be focal narrowing of the cavernous portion of the internal carotid artery (ICA) [7, 8].

Recent reviews argue that, pathophysiologically, THS may not be a single entity but part of a continuum of idiopathic hypertrophic pachymeningitis and idiopathic orbital inflammation. They often talk about: “Classical” / radiologically proven THS, which meets full ICHD-3 criteria with cavernous sinus/orbital granulomatous inflammation on MRI; “Benign” THS (normal-MRI THS) that has a clinical picture typical for THS but no cavernous sinus lesion visible on MRI. Dutta et al. suggest this may reflect imaging limitations or early disease, and propose viewing THS as a focal idiopathic pachymeningitis; idiopathic inflammatory orbital pseudotumor may be its “anterior variant”; THS-like secondary painful ophthalmoplegia, where THS “mimics” where similar painful ophthalmoplegia is caused by lymphoma, infection, vasculitis, sarcoidosis, IgG4-related disease, neoplasm, etc. – i.e. not idiopathic, so by definition *not* “true” THS [7]. Corticosteroid therapy remains the mainstay of treatment, typically producing rapid symptom resolution. Recommended therapy for severe presentations includes high-dose intravenous methylprednisolone (1000 mg daily for 3–5 days) followed by an oral prednisone taper guided by clinical response. In cases of relapse or steroid resistance, immunomodulatory agents such as azathioprine, cyclosporine, methotrexate, mycophenolate mofetil, infliximab, or radiotherapy may be employed as second-line or steroid-sparing therapies. Infectious etiologies should be excluded before initiating corticosteroids, and meningeal biopsy may be considered when the underlying cause remains unclear [1, 9].

Conclusion: Tolosa Hunt syndrome is a rare medical occurrence and a diagnosis of exclusion, and needs to be considered when there is no other cause that impacts cavernous sinus.

References:

1. Thu PW, Chen YM, Liu WM. Recurrent Tolosa–Hunt syndrome. *Tzu Chi Med J.* 2020;33(3):314-316. doi:10.4103/tcmj.tcmj_137_20
2. La Mantia L, Curone M, Rapoport AM, Bussone G. Tolosa–Hunt syndrome: critical literature review based on IHS 2004 criteria. *Cephalalgia.* 2006;26(7):772-781. doi:10.1111/j.1468-2982.2006.01115.x
3. Hunt WE. Tolosa–Hunt syndrome: one cause of painful ophthalmoplegia. *J Neurosurg.* 1976;44(5):544–549.
4. Parisi P, Belcastro V, Verrotti A, Striano P, Kasteleijn-Nolst Trenité DGA. "Ictal epileptic headache" and the revised International Headache Classification (ICHD-3) published in Cephalalgia 2018, vol. 38(1) 1-211: not just a matter of definition! *Epilepsy Behav.* 2018;87:243-245.
5. Hao R, He Y, Zhang H, Zhang W, Li X, Ke Y. The evaluation of ICHD-3 beta diagnostic criteria for Tolosa–Hunt syndrome: a study of 22 cases of Tolosa–Hunt syndrome. *Neurol Sci.* 2015;36(6):899-905.
6. Ramirez JA, Ramirez Marquez E, Torres G, Muns Aponte C, Labat EJ. Tolosa–Hunt syndrome: MRI findings. *Radiology Case Reports.* 2012;7(4):1-6.
7. Dutta P, Anand K. Tolosa–Hunt syndrome: a review of diagnostic criteria and unresolved issues. *J Curr Ophthalmol.* 2021;33(2):104–111.
8. Amrutkar CV, Lui F, Burton EV. Tolosa-Hunt Syndrome. [Updated 2025 Jun 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459225/?utm_source=chatgpt.com
9. Carroll CG, Campbell WW. Multiple cranial neuropathies. *Semin Neurol.* 2009;29(1):53-65.